

a⁶ --The other antiatherosclerotic agent employed in the methods of the invention include MTP inhibitors disclosed in U.S. Patent Nos. 5,595,872, 5,739,135, 5,712,279, 5,760,246, 5,827,875, 5,885,983 and 5,962,440. Preferred are each of the preferred MTP inhibitors disclosed in each of the above patents.--

In the Claims:

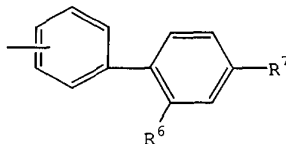
a⁷ 3. (Amended) The method as defined in Claim 1 wherein the aP2 inhibitor contains a hydrogen bond donator or acceptor group and interacts directly or through an intervening water molecule either by ionic or hydrogen bonding interactions, with one, two, or three of the three amino acid residues, designated as Arg 106, Arg 126 and Tyr 128 in human aP2 within the aP2 protein (SEQ ID NO:1).

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Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version With Marking to Show Changes Made". These amendments add no new matter.

REMARKS

Applicants have amended the paragraph beginning at page 6, line 22 of the specification to insert the following chemical structure:



Support for this amendment can be found in the priority document (U.S. provisional application Serial No. 60/100,677, filed September 17, 1998) at page 5 line 24.

Respectfully submitted,

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Version with Markings to Show Changes Made

Page 1, line 3, has been amended as follows please see attachment for marked up version.

This application is a continuation of U.S. Serial No. 09/390,275 filed September 7, 1999, which claims priority from U.S. Provisional Application Serial No. 60/100,677. The entirety of each of these applications is incorporated herein by reference.

Page 3, the paragraph beginning at line 1 and ending at line 16 has been amended as follows:

The aP2 inhibitors suitable for use in the method of the invention are compounds which bind to the aP2 protein (SEQ ID NO:1) and inhibits its function and/or its ability to bind free fatty acids. The compounds will preferably contain less than 60 carbon atoms, more preferably less than 45 carbon atoms, and will contain less than 20 heteroatoms, more preferably less than 12 heteroatoms. They contain a hydrogen bond donator or acceptor group, preferably acidic in nature, which includes, but is not limited to, CO₂H, tetrazole, SO₃H, PO₃H, P(R)(O)OH (where R is lower alkyl or lower alkoxy), OH, NHSO₂R' or CONHSO₂R' (where R' is lower alkyl), and thiazolidindione, and interacts (directly or through an intervening water molecule), either by ionic or hydrogen bonding interactions, with one, two, or three of the three amino acid residues, designated as Arg 106, Arg 126 and Tyr 128 in human aP2, within the aP2 protein (SEQ ID NO:1).

Page 3, the paragraph beginning at line 25 and ending at line 32 has been amended as follows:

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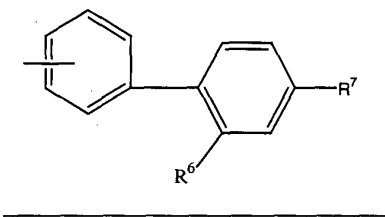
The hydrophobic substituent binds to (in) and/or interacts with a discrete pocket within the aP2 protein (SEQ ID NO:1) defined roughly by the amino acid residues Phe 16, Tyr 19, Met 20, Val 23, Val 25, Ala 33, Phe 57, Thr 74, Ala 75, Asp 76, Arg 78 in human aP2. The through space distance from the hydrogen bond donor/acceptor group and the additional substituent group is within the distance of about 7 to about 15 Angstroms.

Page 4, the paragraph beginning at line 11 and ending at line 13 has been amended as follows:

The accompanying Figure 1 is a computer generated image of a partial X-ray structure of compound XVIA (described hereinafter) bound to human aP2.

Page 6, the paragraph beginning at line 22 and ending at line 24 has been amended as follows:

Preferred are the examples where A is defined as above and B is



Page 28, paragraph beginning at line 21 and ending at line 29 has been amended as follows:

The other antiatherosclerotic agent employed in the methods of the invention include MTP inhibitors disclosed in [in] U.S. Patent Nos. 5,595,872, [U.S. Patent No.] 5,739,135, [U.S. Patent No.] 5,712,279, [U.S. Patent No.] 5,760,246[U.S. Patent No.], 5,827,875, 5[U.S. Patent No.],885,983 and [U.S. Application Serial No. 09/175,180 filed

October 20, 1998, now U.S. Patent No.] 5,962,440. Preferred are each of the preferred MTP inhibitors disclosed in each of the above patents[and applications].

In the Claims:

3. (Amend) The method as defined in Claim 1 wherein the aP2 inhibitor contains a hydrogen bond donator or acceptor group and interacts directly or through an intervening water molecule either by ionic or hydrogen bonding interactions, with one, two, or three of the three amino acid residues, designated as Arg 106, Arg 126 and Tyr 128 in human aP2 within the aP2 protein (SEQ ID NO:1).

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